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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/554,784	06/05/2000	MARK DE BOER	DEBOER2	1336

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EXAMINER
ROARK, JESSICA H

ART UNIT	PAPER NUMBER
1644	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/554,784	Applicant(s) DE BOER ET AL.	
	Examiner Jessica H. Roark	Art Unit 1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 July 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *11,12,17 and 23-28* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *11,12,17 and 23-28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *05 June 2000* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Applicant's proposed amendment after final, filed 7/18/03 (Paper No. 23), is acknowledged and has been entered.

Claims 1-10, 13-16 and 18-22 are canceled.
Claims 23-28 have been added.
Claims 11-12 and 17 have been amended.
Claims 11-12, 17 and 23-28 *are pending.*

2. The indicated allowability of claims 11-12 and 17 is withdrawn in view of the newly discovered references to Gubler et al. (EP0759466, of record) in view of Cohen et al. (WO97/02016) and Trembleau et al. (Immunol. Today 1995; 16(8):383-386). Rejections based on the newly cited references follow.

Accordingly, the finality of the previous Office Action is withdrawn and this Office Action is non-final.

3. *Claims* 11-12, 17 and 23-28 *are under consideration in the instant application.*

Drawings

4. The drawings submitted 6/5/00 have been approved by the Draftsman.

Priority

5. Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

IDS

6. Applicant's IDS, filed 7/5/00 (Paper No. 5), is acknowledged by the current Examiner. An initialed copy of the PTO-1449 was previously provided as part of Paper No. 14.

Specification

7. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention ~~*to which the claims are directed.*~~

8. The Abstract provided as part of the amendment filed 7/12/02 is objected to for the following informality: in the second line, it appears "biding" should be -- binding --. Appropriate correction is required.

9. The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which Applicant may become aware in the specification.

10. The specification is objected to as failing to provide proper antecedent basis for the claimed subject matter. See 37 CFR 1.75(d)(1) and MPEP 608.01(o). Correction of the following is required:

Applicant is requested to identify the written support for claims 12, 24 and 27, particularly the claimed limitation of "a heat shock protein".

It is acknowledged that the original claims provide support for this limitation; however, there must be antecedent basis for the claimed limitation in the specification. Please see MPEP 608.01(o).

Claim Objections

11. Claims 11, 23 and 26 are objected to because of the following informalities: the components of the composition are presented in a confusing fashion. It is suggested that the clarity of the claims could be improved by setting forth the two components in subsections (a) and (b).

Claim Rejections - 35 USC § 112 first paragraph

12. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

13. Claims 11, 12, 17 and 23-28 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. The following *written description* rejection is set forth herein.

The claims recite "a peptide fragment of an autoantigen, or a modified form of an autoantigen" as part of the invention. The specification discloses on page 7 at lines 3-12 several autoantigens, including myelin basic protein, collagen type II, human cartilage glycoprotein 39, insulin, glutamic acid decarboxylase and alpha-fodrin. The specification further discloses on page 7 at lines 3-12 that for therapeutic uses, these autoantigens may be administered in their native form, or that they may be modified by selected amino acid substitutions or used a peptide fragments which may also include selected amino acid substitutions.

The Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement make clear that the written description requirement for a claimed genus may be satisfied by disclosure of relevant, identifying characteristics, i.e., structure or other physical and or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the genus (Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001, see especially page 1106 3rd column).

Although the specification discloses several autoantigens, the specification does not disclose any common structure shared by these disclosed autoantigens that must be shared with other modified autoantigens or peptides thereof.

In addition, the genus of modified autoantigens or peptides thereof is structurally a highly diverse genus. When there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus. Thus even though the specification refers to certain species of modified autoantigen or peptide thereof, these few species, limited to certain variants of one particular autoantigen, do not appear to provide an adequate written description of the extensive genus drawn to *any* modified form of *any* autoantigen or peptides thereof.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the written description inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.). Consequently, Applicant was not in possession of the instant claimed invention. See Regents of the University of California v. Eli Lilly and Co. 43 USPQ2d 1398.

Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

Applicant is invited to point to clear support or specific examples of the claimed invention in the specification as-filed.

Claim Rejections – 35 U.S.C. § 103

14. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

15. Claims 11-12, 17 and 23-28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gubler et al. (EP0759466, of record) in view of Cohen et al. (WO97/02016) and Trembleau et al. (Immunol. Today 1995; 16(8):383-386).

The claims are drawn to compositions comprising a monoclonal antibody or fragment thereof that binds the IL-12R β2 chain expressed on human T cells and having certain functional properties, and comprising an autoantigen, a peptide fragment of an autoantigen or a modified form of an autoantigen. The dependent claims further define the autoantigen and further recite that the composition comprise a physiologically acceptable excipient, diluent, stabilizing agent or carrier.

Gubler et al. teach monoclonal antibodies and fragments thereof which bind the human IL-12 beta2 receptor protein and their application in preventing or treating pathological conditions caused by excess activity of cells expressing IL-12 receptors by inhibiting binding of IL-12 to such cells (see entire document, but especially page 7 at line 56 to page 9 at line 42).

Although Gubler et al. do not teach that the anti-IL-12Rβ2 antibodies prevented IL-12Rβ2 chain-mediated STAT4 phosphorylation or prevented the IL-12Rβ2 chain from dimerizing with the IL-12Rβ1 chain, these properties would be intrinsic in an IL-12Rβ2 antibody that blocked IL-12 activity.

Gubler et al. also teach that the IL-12Rβ2 chain is expressed on the surface of activated T cells (e.g., page 8 at line 56 to page 9 at line 1).

Gubler et al. further teach that the antibody can be used to treat autoimmune dysfunction in diseases including rheumatoid arthritis and multiple sclerosis (page 8 at lines 9-12), and that the antibodies can be administered parenterally as part of a preparation comprising sterile aqueous or non-aqueous solutions, suspensions and emulsions (page 8 at lines 23-49).

Thus Gubler et al. teach compositions comprising an antibody or fragment thereof that binds human IL-12Rβ2 expressed on the surface of human T cells, wherein said composition comprises a physiologically acceptable excipient, diluent, stabilizing agent or carrier.

Gubler et al. do not teach that the composition comprising an antibody or fragment thereof that binds human IL-12Rβ2 expressed on the surface of human T cells, wherein said composition comprises a physiologically acceptable excipient, diluent, stabilizing agent or carrier, should also comprise an autoantigen, a peptide fragment of an autoantigen, or a modified form of an autoantigen.

However, Cohen et al. teach that agents which promote a shift in T cell responses from a TH1 to TH2 type of response can be used in the therapy of autoimmune diseases mediated by TH1 T cells when the agent is administered along with a peptide specific for the autoimmune disease to be treated (see entire document, but especially pages 8-9).

Cohen et al. teach that diseases which could be treated by shifting the T cell mediated response from a TH1 to a TH2 type of response include IDDM (diabetes), rheumatoid arthritis, multiple sclerosis and thyroiditis (page 9 at lines 13-25). Cohen et al. teach examples of peptides that may be used include the p277 peptide of a heat shock protein or peptides from glutamic acid decarboxylase (page 9 at lines 19-20 and page 2 at lines 8-32) for the therapy of IDDM and myelin basic protein peptides for the therapy of multiple sclerosis.

Trembleau et al review the role of IL-12 in induction of organ-specific autoimmune diseases (see entire document). Trembleau e al. teach that because many autoimmune diseases involve a TH1-type of response from T cells and IL-12 induces the development of TH1 T cells, antagonists of IL-12 can be used to treat autoimmune diseases by shifting the TH1 T cell response to a TH2 type of response, including the autoimmune EAE, which is an animal model of multiple sclerosis (see entire document).

Trembleau et al. teach that antibodies to the IL-12R can be used as antagonists of IL-12 function for the for the treatment of autoimmune diseases (see especially page 385, first partial paragraph).

Thus the ordinary artisan at the time the invention was made would have found it obvious to provide a composition comprising an antibody or fragment thereof that binds human IL-12Rβ2 expressed on the surface of human T cells, wherein said composition comprises a physiologically acceptable excipient, diluent, stabilizing agent or carrier, should also comprise an autoantigen, a peptide fragment of an autoantigen, or a modified form of an autoantigen. Gubler et al. teach all components of the composition except the autoantigen, a peptide fragment of an autoantigen, or a modified form of an autoantigen. However, Gubler et al. clearly teach the application of the antibodies and compositions comprising to the treatment of autoimmune diseases, including the autoimmune diseases rheumatoid arthritis (RA) and multiple sclerosis (MS). Cohen et al. teach that RA and MS can be treated using agents that cause a shift in the T cell response from a TH1 to a TH2 type of response by providing the agent in combination with peptides from autoantigens. Trembleau et al. identify antibodies to the IL-12R as agents which can mediate the TH1 to TH2 shift, and once again teach the application of such agents in the treatment of autoimmune diseases.

In view of the combined teachings of the references, the ordinary artisan at the time the invention was made would have been motivated to combine the antibody composition taught by Gubler et al. with any of a number of peptides or intact autoantigens for the treatment of autoimmune diseases by promoting a shift in the T cell response from a TH1 to a TH2 type of response. Cohen et al. teach several peptides which could be used in combination with an agent that promoted a TH1 to TH2 shift. Other peptides and autoantigens were well known in the art at the time the invention was made, including collagen type II, human glycoprotein 39, insulin and alpha fodrin.

Given each component of the composition recited in the prior art and the motivation for combining them, the ordinary artisan at the time the invention was made would have had a reasonable expectation of formulating the instantly recited compositions. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Conclusion

16. No claim is allowed.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jessica Roark, whose telephone number is (703) 605-1209. The examiner can normally be reached Monday to Friday from 8:00 to 4:30. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached at (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center number for before Final submissions is (703) 872-9306.

Jessica Roark, Ph.D.
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Technology Center 1600
August 13, 2003

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